



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
|-----------------|-------------|----------------------|---------------------|------------------|

10/589,216

01/15/2008

Lloyd S. Gray

1036.115US1

5782

21186

7590

12/09/2010

SCHWEGMAN, LUNDBERG & WOESSNER, P.A.

P.O. BOX 2938

MINNEAPOLIS, MN 55402

EXAMINER

XIAO, YAN

ART UNIT

PAPER NUMBER

4111

NOTIFICATION DATE

DELIVERY MODE

12/09/2010

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspto@slwip.com

request@slwip.com

|                              |                                      |                                    |  |
|------------------------------|--------------------------------------|------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/589,216 | <b>Applicant(s)</b><br>GRAY ET AL. |  |
|                              | <b>Examiner</b><br>YAN XIAO          | <b>Art Unit</b><br>4111            |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☐ Responsive to communication(s) filed on 15 January 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 7-12 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 7-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on 11 August 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>09/09/2010,03/03/2010,07/21/2008,01/16/2007.</u> | 6) <input type="checkbox"/> Other: _____  |

Art Unit: 4111

### **DETAILED ACTION**

The Election filed 09/03/2010 in response to the Office Action of 03/09/2010 is acknowledged and has been entered.

Applicant's election with traverse of Group 9, claims 7-12 is acknowledged. Applicant's election of species, mibefradil, without traverse, is acknowledged. Applicant submits that claims 13-15 should be search and examined along with the claims of Group 9 (claims 7-12). Because claims 13-15 related other diseases instead of cancer, claims 13-15 should not be included in group 9 from further consideration by the examiner.

As provided in 37 CFR 1.475(a), an international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention").

1. The groups of inventions do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: There are no common technical features with the claims of the other groups that represent an advance of the art because claims 7, 10, and 11 do not represent an advance over the prior art. See the rejections of claims 7, 10, and 11 below.

For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 7-12 are pending.

Claims 1-6, and 13-15 have been withdrawn from further consideration by the examiner under 37 CFR 1.475(a) as being drawn to non-elected inventions.

### ***Claim Rejections - 35 USC § 102***

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11-12 are rejected under 35 U.S.C. 102 (b) as anticipated by Bertolesi et al. (Mol. Pharmacol. 62:210–219, 2002, hereafter Bertolesi).

Bertolesi teaches mibefradil is distinguished from other  $\text{Ca}^{2+}$  channel antagonists because it preferentially blocks low-voltage-activated T-type  $\text{Ca}^{2+}$  channels (page 210, paragraph 1, line 3-7), it means that mibefradil can inhibit T type  $\text{Ca}^{2+}$  channel of electrically non-excitabile cells; and also teaches that MCF7 breast cancer cells are epithelial cells (abstract).

### ***Claim Rejections - 35 USC § 103***

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 7-8 and 10 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Bertolesi et al. (Mol. Pharmacol. 62:210–219, 2002, hereafter Bertolesi) ) in view of Gray et al. (U. S. Patent Number 6413967, hereafter '967)

Claims 7-8 and 10: Bertolesi teaches mibefradil has additive effects on T type  $\text{Ca}^{2+}$  channel current inhibition (abstract), this meets with claim 7; Mibefradil is a benzimidazolyl-substituted tetraline derivative (page 210, paragraph 1, line 3), this meets claims 8; Mibefradil has also been reported to inhibit the proliferation of various cell types, including blood mononuclear cells, rat smooth muscle cells, mouse liver cells, endothelial cells and retinoblastoma and MCF7 breast cancer cells (Fig.1), this meets with claim 10; Mibefradil was reported to prevent neointima formation after vascular injury in rats (page 218, paragraph 2, line 1-11); Mibefradil induces cell death in retinoblastoma and MCF7 breast cancer cells by different pathways, the mechanism of cell death was primarily necrotic and largely dependent on block of T type  $\text{Ca}^{2+}$

Art Unit: 4111

channels (page 217, right column of the first paragraph, line 15-18). The limitation of Bertolesi is that the treatment and prevention of cancer cells is for cancer patient.

Bertolesi doesn't teach cancer patient.

'967 teaches lymphocytes, epithelial cells, connective tissue cells, secretory cells and PC-3 (a prostate cancer cell line) which lack the type of electrical activity occurring in electrically excitable cells and so are named "electrically non-excitable"; the calcium channels in these types of cell are also referred to as voltage gated (VG) channels by the inventors [BACKGROUND OF THE INVENTION, Column 1, line 45-49; DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS, column 5, line 34-38]; for inhibiting calcium entry into electrically non-excitable cells with said VG-selective inhibitors, methods for preventing proliferation of electrically non-excitable cells with said VG-selective inhibitors as well as methods of treating cancer (abstract). '967 further teaches that "treating" means ameliorating a disease such that the condition of the patient improves or such that the progress of the disease is slowed, the beneficial effects of the VG-selective inhibitors of the present invention can be determined by monitoring an improvement in one or more symptoms; for example, by monitoring the decrease in proliferation (cancer) [DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS, column 10, line 55-61]; these statements meet claims 7-8 and 10 which administering to a patient. The limitation of '967 is that it doesn't teach the inhibitor is mibefradil. Therefore, it would have been obvious to have the mibefradil to inhibit T type calcium channel cancer cells proliferation of Bertolesi taught with electrically non-excitable cells (lymphocytes and epithelial cells *et*) and treatment of cancer patient as taught by '967, because '967 satisfies the limitation of Bertolesi taught.

Claims 9 is rejected under 35 U.S.C. 103 (a) as being unpatentable over Bertolesi et al. (Mol. Pharmacol. 62:210-219, 2002, hereafter Bertolesi) ) in view of Gray et al. (U. S. Patent Number 6413967, hereafter '967), as applied to claim 7 above, and further in view of Lewin et al. (U. S. Patent Application Publication 2006/0110332, hereafter '332).

Art Unit: 4111

Claim 9: Bertolesi and Gray '967 are discussed above, but do not teach that the mibefradil is in dihydrochloride form. '332 teaches using T type calcium channel inhibitor- mibefradil to treat cancer pain; the mibefradil can be applied in any pharmaceutically acceptable salts [0019]. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have mibefradil dihydrochloride salt will be easily uptake by cells.

The combination of Bertolesi, '967 and '332 teaches that the mibefradil can inhibit proliferation of various cell types included cancer cells and prevent neointima formation after vascular injury, therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made that the mibefradil has potential ability to treat cancer patient.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to YAN XIAO whose telephone number is (571)270-3578. The examiner can normally be reached on 5/4/9.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Cleveland can be reached on 571-272-1418. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Application/Control Number: 10/589,216

Page 6

Art Unit: 4111

/YAN XIAO/

Examiner, Art Unit 4111

/Michael Cleveland/

Supervisory Patent Examiner, Art Unit 1712